

Koch Institute for Integrative Cancer Research at MIT

Goals, Objectives, and Priorities

The Koch Institute for Integrative Cancer Research at MIT (KI), a National Cancer Institute (NCI)-designated cancer center, is the hub of cancer research on the MIT campus. The Koch Institute's state-of-the-art facility provides for the physical co-localization of faculty members from MIT's Department of Biology and a variety of departments in the MIT School of Engineering. This multidisciplinary group of investigators is at the core of our mission: to combine science and engineering to develop new insights into cancer as well as new tools and technologies to better diagnose, treat, and prevent the disease.

As a group, our goal is to make the KI the gold standard in interdisciplinary disease-focused research. The organization is continually expanding a highly effective relationship network that involves academic and clinical oncology centers, industrial partners, and cancer-focused individuals and foundations. As part of an institution of higher education, we are also deeply committed to training the next generation of cancer researchers.

In this reporting period, the ongoing global Covid-19 pandemic presented unique challenges to research and training opportunities; however, KI laboratories, trainees, and administrative staff continued to move their research and administrative work forward by working remotely where possible and, for approved personnel, in person. As with other research and academic units at MIT, the KI was able to bring its research activities to 100% capacity in October. Opportunities for collaboration, engagement, and connection continued to be available via virtual, in-person, and hybrid environments.

The Koch Institute is grateful to MIT, the members of the Research Continuity Working Group, the Research Ramp Up "Lightning" Committee (which included David H. Koch Professor of Biology and former KI director Tyler Jacks and Virginia and D.K. Ludwig Professor for Cancer Research and associate director Jacqueline Lees, as well as senior KI administrators Sarah Farrington and Vasilena Gocheva), and the Research Ramp Up "Thunder" Committee for their expertise, guidance, and tireless work to develop processes and procedures to protect the health and safety of KI researchers and staff, allowing us to continue our important work.

Finances and Funding

Funding for research performed within the KI building comes from several sources, including federal grants, philanthropic gifts, and industrial contracts. The total was more than \$87 million in FY2021. This figure is based on intramural faculty expenditures and includes total sponsored research volume, philanthropic funding, funding for five Howard Hughes Medical Institute faculty members, corporate funds, faculty discretionary account spending (mostly from chair accounts), postdoctoral and graduate fellowship funding through various MIT mechanisms, core facility chargeback accounts, and MIT general budget allocations. Also included are funds managed by the KI for specific cancer research efforts across MIT.

Critical to cancer research on the MIT campus is the NCI Cancer Center designation, which MIT—first through the Center for Cancer Research and now through the KI—has held since 1974. The Cancer Center Support Grant is re-competed every five to seven years via a grant application and a site visit from the NCI. Our renewal was successfully completed in October 2019 with a perfect score of 10, and the NCI recommended approval of the budget at the requested amounts.

The interdisciplinary nature of the research conducted at the KI has resulted in faculty members participating in many multi-investigator collaborative projects. Examples include those funded by grants from the NCI, such as the Physical Science-Oncology Center, the MIT-Harvard Center of Cancer Nanotechnology Excellence, the Tumor Cell Networks Center (formerly the Integrated Cancer Biology Program), and the Tumor Microenvironment Network.

Research Centers and Initiatives

The Koch Institute has been successful in identifying and negotiating funding from individuals, foundations, and companies in support of its research mission. Several philanthropically funded cancer-focused centers and initiatives have been established at the KI:

The Ludwig Center at MIT was established in 2006 with a gift from the Virginia and D.K. Ludwig Fund for Cancer Research. With a focus on understanding and disrupting the process of tumor metastasis, it currently provides partial research support for nine KI faculty members while also providing fellowships for students and postdocs.

The Marble Center for Cancer Nanomedicine is an endowed center that was launched in the spring of 2016 through the generosity of Curt Marble '63 and his late wife, Kathy. The center's inaugural director is Sangeeta Bhatia, the John J. and Dorothy Wilson Professor of Health Sciences and Technology. The center brings together six of the KI's engineering faculty members to focus on grand challenges in cancer diagnosis and treatment that could benefit from interventions at the nanoscale: detecting cancer earlier than existing methods allow, harnessing the immune system to fight cancer even as it evolves, exploiting therapeutic insights from cancer genomics to design therapies for previously undruggable targets, combining existing drugs for synergistic action, and creating tools for better surgical intervention. The center provides important fellowship support and training opportunities for the next generation of nanoscientists and nanoengineers, and collaborative opportunities for all members.

The MIT Center for Precision Cancer Medicine (CPCM) was launched in 2017 through the generosity of an anonymous donor, and is focused on translational research to help patients who do not respond well to existing therapeutic approaches. By focusing on how to select the right targets to treat cancer in each patient, CPCM investigators are working to significantly alter patient outcomes by determining the right combination of therapies for a particular patient and developing innovative ways to give drugs, be it time-staggered dosages or formulations that target the therapy directly to the tumor. In addition, the center concentrates its research efforts on identifying mechanisms that determine an individual's response to therapy and on targeting hard-to-drug targets and identifying novel vulnerabilities created by cancer cells' adaptations to stress. Michael

Yaffe, the David H. Koch Professor in Science, is the center's inaugural director. He is joined by five additional KI members.

The MIT Stem Cell Initiative was launched in 2018 with generous philanthropic support. The initiative's goal is to understand the biology of normal adult stem cells and cancer stem cells. Led by Professor Jacqueline Lees, its faculty also includes Eisen and Chang Career Development Associate Professor of Biology Ömer Yilmaz, Daniel K. Ludwig Professor for Cancer Research Robert Weinberg, and Associate Professor Alex Shalek. The initiative conducts a program of pilot projects to expand its faculty and collaborative network as well as technological resources to support stem cell research at MIT. Examples of the latter include construction of an oblique-plane microscope for longitudinal monitoring of organoid models in the Robert A. Swanson (1969) Biotechnology Center's Microscopy Core Facility, and equipment and training for its Barbara K. Ostrom (1978) Bioinformatics and Computing Facility and Genomics Facility to improve single-cell RNA sequencing capabilities. As the Swanson Center is open to the entire MIT community, these efforts have greatly expanded MIT's overall access to cutting-edge technologies.

The Lustgarten Laboratory for Pancreatic Cancer Research at MIT was established in 2019 with \$5 million in support from the Lustgarten Foundation. Headed by Professor Jacks, the lab reflects MIT's commitment to researching pancreatic cancer, the fourth leading cause of cancer mortality in the US. The lab seeks to better understand the immunological conditions and genetic events that contribute to the development of pancreatic cancer, to study the disease on a single-cell level in both humans and mouse models, and to develop novel high-throughput tools for culture and drug testing using organoid models. The Lustgarten Foundation's investment supports postdocs, graduate students, technicians, and a senior scientist.

Partnerships and Programs

The KI has multiple initiatives to ensure that its innovative research is translated from bench to bedside and will benefit cancer patients.

The Koch Institute Frontier Research Program supports exciting proof-of-concept, interdisciplinary investigations and collaborations since such early-stage ideas often do not qualify for funding from traditional sources. The Frontier Research Program, which is funded solely through philanthropy, represents an investment in the future and highlights the far-reaching vision of the KI community. Examples of projects include engineered complexes that flag challenging molecular disease targets for disposal by the cellular waste management system, devices to enable oxygen-based customization of radiation therapy dosing, injectable nanoparticles that create urinary biomarkers to reveal the presence of cancer within minutes, and an imaging system for early detection and surgical resection of ovarian tumors smaller than a millimeter in diameter. Several Frontier-funded projects have resulted in intellectual property and the founding of new companies and are being translated to help patients in the clinic.

The Bridge Project provides additional opportunities for faculty members to develop research toward clinical and commercial applications via collaborations with clinical

partners. The Bridge Project partnership with Dana-Farber/Harvard Cancer Center (DF/HCC)—comprising all five Harvard teaching hospitals and its medical and public health schools—is designed to support inter-institutional cancer research efforts of faculty members at MIT and Harvard. Launched in 2012, the Bridge Project has given more than 65 awards to research teams that are developing new treatment and diagnostic methods for various cancers. The project is funded exclusively by philanthropic gifts, raised collaboratively by the KI and DF/HCC development teams. A new five-year \$25 million challenge gift was secured in 2021 from the Commonwealth Foundation for Cancer Research, and will provide substantial funding for the program over the next several years. Outcomes from Bridge Project teams include joint publications in peer-reviewed journals, patent applications, and follow-on funding from the National Institutes of Health, the NCI, the Department of Defense, and charitable foundations. To date, 13 Bridge teams have advanced their research to the point where ideas are being tested in the clinic or are close to clinical trials, and seven new companies have emerged based on Bridge Project intellectual property.

The KI's network of research relationships has involved more than a dozen companies in its first decade, including relationships with Takeda Oncology and Janssen Pharmaceuticals—the pharmaceutical division of Johnson & Johnson. Growing this network of industry relationships remains an ongoing priority for the Koch Institute in order to enhance the impact of its research portfolio.

Trainee Support

Additional programs support the training of the next generation of cancer researchers. By providing training opportunities for professional development beyond the bench and recognizing the critical role of mentorship in academic pursuits, these programs aim to recruit and retain people with both science and engineering backgrounds.

The Convergence Scholars Program helps postdoctoral fellows and associates build experience and capacity by coordinating group activities to develop skills in leadership, communication, management, and translational impact, and by offering a variety of options for individual professional development and engagement with industry and clinicians. Started in 2017 with six scholars, the class of AY2021 included 12 postdoctoral members, six each from the Marble Center and from the MIT Center for Precision Cancer Medicine. Because of limits on in-person activities due to the pandemic, the last cohort will be retained for an additional year alongside a new cohort for AY2022.

The Peter Karches Mentorship Prize has been awarded annually since 2018 in recognition of the important role postdoctoral researchers and graduate students play in the mentorship of high school and undergraduate students working in KI laboratories. Each year, four trainees are honored with the award, for which they are nominated by their mentees and supported by their faculty advisor.

Personnel Information

A number of significant personnel changes occurred this year, most notably the appointment of a new Koch Institute director. After nearly 20 years as director of MIT's cancer research community, and over a decade as the first director of the Koch Institute,

Professor Jacks announced in the fall that he would step down from the post. Matthew Vander Heiden, the Lester Wolfe (1919) Professor of Molecular Biology, who previously served as an associate director of the KI, assumed the role of director in April 2021. Professor Vander Heiden, whose lab focuses on cancer metabolism, is the first practicing oncologist to serve in this role.

In the spring, Paula Hammond, head of the Department of Chemical Engineering, was named an Institute Professor in recognition of her many contributions to research, teaching, and community leadership. Additionally, the Koch Institute brought on board a new executive director, Jane Wilkinson.

Sadly, not all of this year's notable events were happy ones—long-time Koch Institute member and Kathleen and Curtis Marble Professor of Cancer Research Angelika Amon, a pioneering biologist, passed away in October 2020 at age 53 due to complications from ovarian cancer.

The KI building currently houses 30 faculty members—14 from the Department of Biology, including two emeriti members; 14 from the School of Engineering, one with a joint Biology/Engineering appointment; and MIT's President Emerita—as well as two clinical investigators. The Johnson Clinical Investigators Program funds two physician-scientists for three to five years, during which they receive dedicated lab space and research support while spending a portion of their time treating patients.

Frank B. Gertler retired and became professor of biology emeritus in 2020.

The Koch Institute includes 34 MIT faculty who are extramural members. Through their involvement in research on cancer or cancer-related subjects, extramural faculty participate in a variety of ways in the research activities of the KI. This year, we added five new extramural faculty members: W. M. Keck Career Development Professor in Biomedical Engineering Kate E. Galloway (Department of Chemical Engineering), Assistant Professor Anders Hansen (Department of Biological Engineering), Novartis Professor of Chemistry Laura Kiessling (Department of Chemistry), Roger and Georges Firmenich Professor of Natural Products Chemistry Ronald T. Raines (Department of Chemistry), and Landon T. Clay Professor of Biology Jonathan Weissman (Department of Biology).

The Swanson Biotechnology Center, which houses the KI's 14 core facilities, is available to the KI community as well as to researchers from around MIT. The center employs approximately 40 KI-appointed full-time staff scientists.

At the end of FY2021, 120 graduate students and 122 postdoctoral fellows or associates had active appointments in KI building faculty laboratories. The Koch Institute's total personnel count is approximately 605.

In order to strengthen the KI's bench-to-bedside focus, the Koch Institute invites a number of research fellows on an annual basis to work in its labs, where they have access to equipment, resources, and mentoring opportunities.

Faculty Honors and Awards

Several KI members were recognized this past year for their contributions to science, technology, and the fight against cancer:

Angelika Amon's work on aneuploidy-induced cellular changes and their contribution to carcinogenesis was recognized with the 2020 Human Frontier Science Program Nakasone Award. She also received the Ernst W. Bertner Memorial Award from MD Anderson.

Delta Electronics Professor Regina Barzilay received the Association for the Advancement of Artificial Intelligence's Squirrel AI Award for Artificial Intelligence for the Benefit of Humanity in 2020 for her work advancing the use of AI in medicine, as well as the Wallace H. Coulter Lectureship Award in 2021 by the American Association Cancer Research (AACR) for her lifetime commitment to and contributions with impact on education, practice, and/or research in laboratory medicine and patient care.

Class of 1956 Career Development Professor Michael Birnbaum received the Damon Runyon-Rachleff Innovator award, the Michelson Prize for Human Immunology and Vaccine Research, and a NIH New Innovators Award, all in 2020.

Y. Eva Tan Professor in Neurotechnology Edward Boyden was awarded the Wilhelm Exner Medal in 2020 for his expansion microscopy work.

Professor Linda Griffith became a member of the American Academy of Arts and Sciences in 2021. She was awarded the Bernard M. Gordon Prize for Innovation in Engineering and Technology Education from the National Academy of Engineering in 2021, along with her KI-extramural-faculty colleague, Ford Professor of Engineering Douglas Lauffenburger.

Anders Hansen, one of our newest KI extramural faculty members, became a Pew-Stewart Scholar for Cancer Research in 2021.

Tyler Jacks was honored with the AACR Princess Takamatsu Memorial Lectureship in 2020.

Institute Professor Rober Langer received the Maurice-Marie Janot Award in 2020 from the Association Pharmaceutique Galénique Industrielle for pioneering work that has a groundbreaking impact in the fields of pharmaceuticals, biopharmaceuticals, and pharmaceutical technology.

Professor Harvey Lodish became a foreign member of the Royal Academy of Medicine of Belgium in 2020.

Professor Aviv Regev received the Lurie Prize in Biomedical Sciences in 2020, as well as the National Academy of Sciences James Prize in Science and Technology Integration in 2021, and became a fellow of the AACR Academy in 2021.

Professor David Sabatini received the BBVA Foundation Frontiers of Knowledge in Biomedicine award, the Sjöberg Prize for his discoveries about cell growth control, and the Mechthild Esser Nemmers Prize in Medical Science from Northwestern University, all in 2020.

Associate Professor Alex Shalek won MIT's 2019–2020 Harold E. Edgerton Faculty Award, which recognizes exceptional distinction in teaching, research, and service.

Institute Professor Phillip Sharp was selected for the AACR Award for Lifetime Achievement in Cancer Research in 2020.

Daniel K. Ludwig Professor for Cancer Research Robert Weinberg was recognized with the Japan Prize for Medical Science and Medicinal Science in 2021, with Dr. Bert Vogelstein from Johns Hopkins University, for their work on the development of a multi-step carcinogenesis model.

Michael Yaffe became a member of the Association of American Physicians in 2021 and was also named a MacVicar Faculty Fellow that year for his exceptional undergraduate teaching.

Publications and Start-up Companies

The KI's portfolio of published research and start-up companies is a testament to the institute's success in bringing scientists and engineers together to encourage interdisciplinary approaches in cancer research.

The KI continues to be the publication center of interdisciplinary cancer research at MIT and across the local research community. In FY2021, KI intramural and extramural researchers produced more than 516 publications; over 13% are joint publications of multiple KI labs.

The entrepreneurial spirit of the KI continues to thrive. More than 100 companies have been started by KI faculty. Led by Koch Institute members Sangeeta Bhatia and Harvey Lodish, the Future Founders Initiative was established this past year, seeking to increase the number of biotech companies in the Boston area founded by women. The initiative builds on Professor Bhatia's recent work with MIT President Emerita Susan Hockfield and Amgen Professor of Biology Emerita Nancy Hopkins around gender disparities in entrepreneurship, focusing on networking and community building.

Koch Institute Community Building

The KI organized a series of primarily virtual activities with the goal of strengthening integration and furthering interactions between scientists and engineers and clinicians within our research community.

Oncology Seminar Series: This cancer-specific seminar series at MIT invites leading cancer researchers and clinicians to present their work and meet with KI faculty and researchers. Over its nine years, the KI has hosted 60 speakers. Due to the pandemic, seminars were suspended during the fall semester but were held virtually in the spring. Four speakers were featured, attracting a substantial audience, and the speakers also met individually with faculty via Zoom.

Yearly Fall Retreat: This retreat provides an off-campus opportunity for sharing lab research and highlighting new research areas through formal presentations, poster sessions, and casual events. Unfortunately, this year's retreat was cancelled due to the pandemic.

Summer Lunch and Learn Seminar Series: With the goal of fostering the next generation of cancer researchers, this seminar series gives MIT's high school and undergraduate summer students an opportunity to hear firsthand from our faculty members about their research and career paths. Pandemic restrictions unfortunately forced the cancellation of last summer's series. In summer 2021, however, six Koch Institute faculty members presented to the trainees in a hybrid format.

Committee for Community Life: KI volunteers (trainees, staff, researchers, and administrators) organize community-building events as well as the seminars and lectures. They also discuss other issues of importance to postdoctoral researchers and graduate students. Examples of special programs this year include:

- *Health and Wellness:* Under the umbrella of the Committee for Community Life, the Health and Wellness subcommittee aims to provide opportunities for everyone in the KI community to develop and maintain healthy lifestyles by supporting the adoption of habits and attitudes that contribute to wellbeing. Opportunities this year have included online self-care wellness/corrective techniques and a meditation workshop.
- *Friday Focus:* This weekly seminar series is a forum for trainees in KI laboratories to present their research to the entire community. This effort has also become a cross-disciplinary educational/training platform that enhances interactions among KI labs. Friday Focus was held virtually during AY2021.

Cancer Community Newsletter: Our electronic newsletter, Changing the Course of Cancer, published since 2009, sends news and highlights of KI members' achievements, awards, and publications to current and past KI members.

The Koch Institute formed a Diversity, Equity, and Inclusion (DEI) Council this year, with the goal of fostering and supporting a diverse, equitable, and inclusive environment, as well as strengthening community and a sense of belonging. The council is composed of faculty, administrators, graduate students, postdocs, and research staff. It provides direction, oversight, and accountability for the execution of the Koch Institute's overall DEI strategy, including the implementation of best practices.

Neel Bardhan, a postdoctoral researcher in the laboratory of Angela Belcher, launched *Let's Get to Know ... Celebrating Diversity at MIT*, a MindHandHeart-funded podcast that invites KI faculty, trainees, and staff from different backgrounds to share their stories and music, food, literature, and more from their respective cultures.

Outreach Activities

The KI continues to focus on outreach beyond its immediate research community.

Koch Institute Public Galleries: These galleries were established to connect the Kendall Square community and beyond with work being done at the cutting edge of cancer research and life sciences work at MIT. Within the galleries, visitors can explore cancer research projects, examine striking biomedical images, hear personal reflections on cancer and cancer research, and investigate the historical, geographical, and scientific contexts

from which the KI emerged. The galleries are free and open to the public on weekdays from 8 am to 6 pm (4 pm on Fridays), but unfortunately had to be closed during AY2021 due to the pandemic. However, we continued with our annual exhibition of the winning life sciences and biomedical images from the Koch Institute Image Awards. This year's winning images were featured in *STAT*, *Cell Picture Show*, and *National Geographic*, among other outlets. Several new exhibits are being planned for the coming year.

Public Lectures: Initiated in September 2011, the KI's signature public lecture series, with/in/sight, features the insights that emerge when science meets engineering, clinical practice meets urgent patient needs, entrepreneurial drive meets venture capital, and imaging technology meets artistic vision. Due to the pandemic, events were held virtually over the past year. Three with/in/sight webinars, showcasing collaborative research and signature programs, were held, along with three sets of Image Awards lightning talks. In addition, the KI hosted a Zoom conversation between MIT President Emerita Susan Hockfield and Matthew Vander Heiden as part of the KI's 10th anniversary celebrations.

School Programs: The KI is committed to fostering an interest in science and engineering in young people. As part of this mission, we invite groups of middle- and high school students (grades 7–12) to visit our facilities, meet our researchers, and learn interactively about the science and technology of cancer research. Although the closure of the MIT campus and challenges within school districts limited the number of groups we could host, the KI was able to offer virtual programming to several community groups, introducing nearly 100 K–12 students to cancer research. KI volunteers played a significant role in these virtual visits, sharing their research, laboratories, and career experiences.

Public Outreach Events: This year's Cambridge Science Festival was hosted entirely online. KI trainees and staff members offered laboratory tours via Zoom and video, sharing behind-the-scenes views of Koch Institute research with 225 visitors and viewers. Additionally, the Koch Institute participated in the MIT Museum's second annual Imaging Science program, celebrating "discovery through photography."

KI Cancer Solutions Newsletter: This monthly electronic newsletter, published since 2009, sends news and highlights of newsworthy achievements, awards, and publications of KI members to more than 5,000 individuals from a variety of constituencies.

Other Programs: Two regular programs were postponed in AY2021 due to the Covid-19 pandemic. The 19th annual cancer research symposium and sixth annual Judith Ann Lippard Memorial Lectureship will both be held in AY2022.

Administrative Initiatives

The Koch Institute's administrative goal is to support and facilitate the work of KI researchers. Administrative initiatives this year revolved primarily around the response to the Covid-19 pandemic and ensuring that our researchers, staff, and trainees could successfully continue their work either remotely, on site, or in a hybrid manner. Specific initiatives included the formation of a Department Monitoring and Compliance Committee (DMC), which met weekly beginning in July, and was charged with ensuring

that the KI followed all MIT guidelines for Research Ramp Up Phase 2 and complied with all safety procedures and lab personnel requirements. The DMC committee members acted as liaisons for constituents in the labs, and set up an anonymous online portal to facilitate reporting concerns and questions related to in-person research activities. The DMC discussed compliance issues and worked with faculty, researchers, staff, and trainees as issues arose. In addition, the DMC provided timely communication to the KI, and took proactive steps to aid the community in understanding and implementing Covid-19-related restrictions and protocols.

In July 2020, the KI initiated an ambassador program of volunteers from the community who assisted in efforts to maximize safety in our building. The ambassadors were on site six days per week, providing information and assistance and making sure that supplies such as disinfectant solutions, gloves, and hand sanitizer were stocked throughout all the common areas.

Finally, senior KI administrators participated in institute endeavors such as Task Force 2021, the personal protective equipment supply chain committee, and the Research Ramp Up “Lightning” Committee.

In Closing

With an intense focus on developing new solutions to the complex challenges of cancer, MIT’s Koch Institute assembles world-class interdisciplinary researchers in a state-of-the-art cancer research and technology facility. Although this was a challenging year, we are grateful to the faculty, researchers, trainees, and staff who worked diligently and tirelessly to continue to leverage the Koch Institute’s collaborative research model and its strengths in cancer biology and cancer-oriented engineering, and accelerate the rate of progress in understanding cancer and bringing innovation to improve the lives of cancer patients.

Matthew Vander Heiden
Director
Lester Wolfe Professor of Molecular Biology